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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/147,770	04/28/1999	PIERO DEL SOLDATO	P8907-9002	2174

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EXAMINER
TRAVERS, RUSSELL S

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 10/21/2002 24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/147,770	Del Soldato et al
Examiner	**Art Unit**
Russell Travers	1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 7, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, and 5-20* is/are pending in the application.

4a) Of the above, claim(s) *6-8 and 11-20* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 5, 9, and 10* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The response and declaration filed August 7, 2002 have been received and entered into the file.

Applicant's arguments filed August 7, 2002 have been fully considered but they are not deemed to be persuasive.

Claims 1-2, and 5-20 are presented for examination.

Applicant's election without traverse of Group I, claims 1-5 in Paper No. 10 is acknowledged.

Claims 6-8, and 11-20 reading on non-elected subject matter are withdrawn from consideration. Claims 1-2, 5, 9 and 10 will be examined to the extent they read on the elected subject matter.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-2, 9 and 10 are rejected under 35 U.S.C. § 103 as being unpatentable over Merck Index #4852, Morikawa et al, Persson et al and Chung et al.

Merck Index #4852 teach indomethacin as old and well known in combination with various pharmaceutical carriers and excipients in a dosage form. This medicament is taught as useful for treating inflammation. Morikawa et al teach indomethacin as old and well known in combination with various pharmaceutical carriers and excipients in a dosage form. Persson et al and Chung et al Morikawa et al teach NO donors as old and well known in combination with various pharmaceutical carriers and excipients in a dosage form. Nitric oxide donors are taught by Persson et al and Chung et al as useful for increasing the time to micturition, and increasing bladder pressure threshold. These medicament are taught individually as useful for increasing the time to micturition, and increasing bladder pressure threshold. Compounds taught as useful for increasing the time to micturition, and increasing bladder pressure would have been seen as useful for treating urinary incontinence by the skilled artisan. Claims 1-2, 9 and 10 , and the primary references, differ as to:

1) the recitation of those medicaments set forth in claims 9 and 10, and

2) concomitant employment of these medicaments

The skilled artisan, possessing a compound for a therapeutic use possesses that compounds analogs, homologs, isomers, bioisosteres, salts, acids and esters for the same use. To employ an analog, homolog, isomer, bioisostere, salts acid and

ester for the same use therapeutic use would have been obvious to the skilled artisan. Prior art use for the same therapeutic purpose would have motivated the skilled artisan to employ indomethacin esters to the same therapeutic use and enjoy a reasonable expectation of therapeutic success.

It is generally considered prima facie obvious to combine two compounds each of which is taught by the prior art to be useful for the same purpose, in order to form a composition which is to be used for the very same purpose. The idea for combining them flows logically from their having been used individually in the prior art. As shown by the recited teachings, the instant claims define nothing more than the concomitant use of conventional anti-detrusor agents. It would follow that the recited claims define prima facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

RESPONSE TO ARGUMENTS

Newly presented rejection renders the instant rebuttal arguments moot.

Applicants declaration filed under 37 CFR 1.132 has been considered, but is unconvincing. Applicants aver unexpected benefits residing in the claimed subject matter, yet fail to fails to set forth evidence substantiating this belief. Evidence as to unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). The data provided by

Applicants is not convincing or reasonably commensurate in scope with the instant claims. It is a well established principle of patent law that no invention resides in combining two or more ingredients of known character, where the results obtained are no more than the additive effect of the individual components. In this regard the data of the declaration and specification has been considered but is not deemed persuasive to over come this prima facie case of obviousness. The data presented is very limited as to the ingredients tested as well as the relative amounts of each in the test compositions. The claims are not so limited.

The evidence necessary to overcome a prima facie case of obviousness must not only be clear and convincing, but commensurate in scope with the claimed subject matter. The allegation that the limited data is sufficient to establish the existence of synergism from other such ingredients is without merit. It is well recognized that synergism is a highly unpredictable result which is very dependant on ingredients used and the amounts of each. Thus, any combination for which synergism is not clearly established, would be properly rejected since non-obviousness would not have been established.

It is well established that where, as here, a synergistic effect is alleged it must be shown, or reasonable basis must exist, that such an effect will be realized with all of the possible combination embraced by the claims. See In re Smith, 55 CCPA 1352, 389 F. 2d 849, 158 USPQ 287 (1968), In re Lemin et al, 56 CCPA 1050, 408 F.2d 1045, 161

USPQ 288 (CCPA 1969), In re Kollman et al, 595 F.2d 48, 201 USPQ 193 (CCPA 1979).

As stated above, the instant claims read on analogs, homologs, isomers, bioisosteres, salts, acids and esters known for the same therapeutic use claimed herein. The skilled artisan possessing the core compounds for the same therapeutic purpose would have motivated the skilled artisan to employ indomethacin esters to the same therapeutic use enjoying a reasonable expectation of therapeutic success.

Attention is directed to page 51 (table 2) setting forth physiological effects of the parent compound and the claimed ester. Although no test for data reliability was offered, Examiner finds only a 10% difference between those effects provided by the parent compound, and the claimed ester. Examiner's 10% difference determination is, by necessity, based on the unlikely situation where no variation was seen between tests: a highly unlikely course of events. Absent a showing of **unexpected** benefits residing in the claimed subject matter, the instant claims remain properly rejected as obvious.

It is well known by the skilled artisan that carriers and excipients are employed to enhance the activity of active ingredients. Thus, the skilled artisan would expect conventional excipients and carriers to be useful concomitantly, absent information to the contrary. The instant carriers and excipients are not employed concomitantly in the prior art, thus only obviate their concomitant use.

Examiner notes synergy is demonstrated by an illustration of physiological effect being greater than additive for those compounds' physiological effects individually.

No claims are allowed.

Any inquiry concerning this communication should be directed to Russell Travers at telephone number (703) 308-4603.

Russell Travers J.D., Ph.D.
Primary Examiner
Art Unit 1617